

Serial No. 10/017,235 - Murphy - Amendment - Abstract

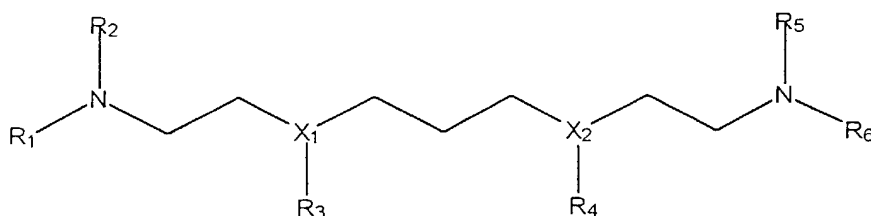
## ATTACHMENT 2

Marked Up Version of The Abstract

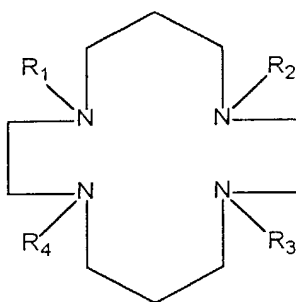
## ABSTRACT

[The invention relates to the preparation of novel therapeutically active polyamine derivatives of 1,3-bis-[(2'-aminoethyl)-amino]propane (2,3,2-tetramine) and 1,4,8,11-tetraazacyclotetradecane (cyclam), optimization of their mechanistic and bioavailability characteristics, which compounds can be used in the treatment of Parkinson's disease, Alzheimer's disease, Lou Gehrig's disease, Binswanger's disease, Olivopontine Cerebellar Degeneration, Lewy Body disease, Diabetes, Stroke, Atherosclerosis, Myocardial Ischemia, Cardiomyopathy, Nephropathy, Ischemia, Glaucoma, Presbycusis and Cancer.

Accordingly, in one aspect the invention is directed to compounds of the formula:



or



Wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, □-lipoic acid, □-tocopherol, ubiquinone, phylloquinone, □-carotene, menadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene – (CH<sub>2</sub>)<sub>n</sub>[XCH<sub>2</sub>]<sub>n</sub>NH<sub>2</sub> - wherein n = 3-6 and X = nitrogen, sulfur, phosphorous or carbon, or heterocycle wherein R<sub>1</sub> and R<sub>2</sub> taken together are –(CH<sub>2</sub>XCH<sub>2</sub>)<sub>n</sub>- wherein n = 3-6 and X = nitrogen, sulfur, phosphorous or carbon.

$R_3$  and  $R_4$  may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol,  $\alpha$ -lipoic acid,  $\alpha$ -tocopherol, ubiquinone, phylloquinone,  $\beta$ -carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene or heterocycle wherein  $R_3$  and  $R_4$  taken together are  $-(CH_2XCH_2)_n-$  wherein  $n = 3-6$  and  $X =$  nitrogen, sulfur, phosphorous or carbon.

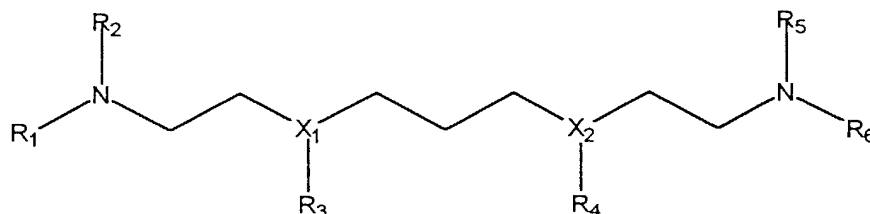
$R_5$  and  $R_6$  may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol,  $\alpha$ -lipoic acid,  $\alpha$ -tocopherol, ubiquinone, phylloquinone,  $\beta$ -carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene -  $(CH_2)_n[XCH_2]_nNH_2$  - wherein  $n = 3-6$  and  $X =$  nitrogen, sulfur, phosphorous or carbon, or heterocycle wherein  $R_5$  and  $R_6$  taken together are  $-(CH_2XCH_2)_n-$  wherein  $n = 3-6$  and  $X =$  nitrogen, sulfur, phosphorous or carbon.

$M$ ,  $n$ , and  $p$  may be the same or different and are bridging groups of variable length from 3-12 carbons.

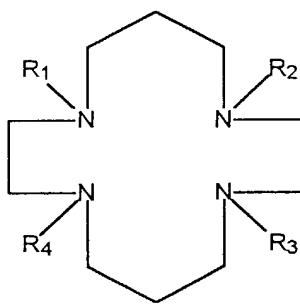
$X_1$  and  $X_2$  may be the same or different and are nitrogen, sulfur, phosphorous or carbon.

The invention relates to the preparation of novel polyamines, such as derivatives of 1,3-bis-[(2'-aminoethyl)-amino]propane (2,3,2-tetramine) and 1,4,8,11-tetraazacyclotetradecane (cyclam), which can be used to treat mitochondrial and degenerative diseases.

Accordingly, in one aspect the invention is directed to compounds of the formula:



or



wherein

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, urate, ascorbate, estrogen, dehydroepiandrosterone, redox stabilizing substituents, a quinone, glutamate, succinate,  $-(CH_2)_n[XCH_2]_nNH_2$  - wherein n = 3-6 and X = nitrogen, sulfur, phosphorous or carbon, or heterocycle wherein R<sub>1</sub> to R<sub>6</sub> taken together are  $-(CH_2XCH_2)_n$  - wherein n = 3-6 and X = nitrogen, sulfur, phosphorous or carbon.

M, n, and p may be the same or different and are bridging groups of variable length from 3-12 carbons.

X<sub>1</sub> and X<sub>2</sub> may be the same or different and are nitrogen, sulfur, phosphorous or carbon.